In the Claims:

Cancel claims 4, 6, 13, 15, 17 and 30, amend claims 1, 2, 3, 7, 12, 14, 18-22, and add new claims 31, 32 and 33 as follows:

1. (Twice Amended) A compound of formula I:

(Y-N)-(spacer)-(amidine or guanidine group),

(I)

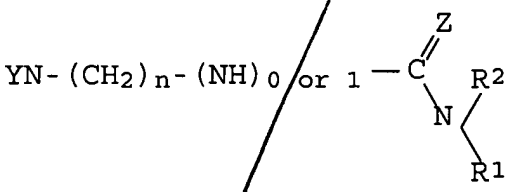
wherein Y-N is an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine, and N in Y-N is a nitrogen atom of said opioid, to which is linked a spacer, which links said compound to an amidine or guanidine group or a pharmaceutically acceptable salt thereof,

wherein said compound acts as an analgesic, and has reduced or no activity in the central nervous system in comparison to said opioid Y-N.

2. (Twice Amended) A compound according to Claim 1, in which the spacer is a straight or branched alkyl, alkenyl or alkynyl chain of 1 to 6 carbon atoms.

3. (Twice Amended) A compound according to Claim 1, in which the spacer is a cyclic alkyl, alkenyl or alkynyl group.

7. (Twice amended) A compound according to Claim 1, of formula (II):



(II)

in which YN- represents an organic residue obtained by removal of the R group from an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine of formula (IIIa)

YN-R

(IIIa)

wherein R is H, alkyl of 1 to 6 carbon atoms, or cyclopropylmethyl,

Z is NR^3;

R^1 is H, alkyl or aryloxyalkyl, wherein the aryl group is optionally substituted by alkyl, alkoxy, halogen, or alkyl substituted by halogen, and alkyl, alkoxy and the alkyl moiety of aryloxy alkyl have 1 to 6 carbon atoms;

R^2 is H or an alkyl group having 1 to 6 carbon atoms;

R^3 is H, alkyl, hydroxy, amino, cyano or acyl, wherein alkyl and acyl have 1 to 6 carbon atoms;

n is an integer of 1 to 6,

and wherein

R^1 and R^3 may together complete a ring,

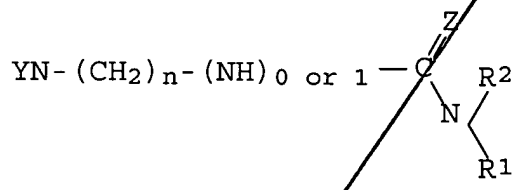
or a pharmaceutically acceptable salt thereof.

12. (Twice Amended) A compound according to Claim 8, in which R^1 and R^2 are both H.

14. (Twice Amended) A compound according to Claim 12, in which the opioid is morphine, codeine or buprenorphine.

18. (Twice Amended) A method of reducing the central nervous system activity of an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine, comprising the step of linking the nitrogen atom of said opioid to a spacer group, which in turn is linked to an amidine or guanidine group.

19. (Twice Amended) A method for the preparation of a compound of formula II



(II)

in which

YN-represents an organic residue obtained by removal of the R group from an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine of formula (IIIa)

YN-R

(IIIa)

wherein R is H, alkyl of 1 to 6 carbon atoms, or cyclopropylmethyl,

Z is NR^3;

R^1 is H, alkyl or aryloxyalkyl, wherein the aryl group is optionally substituted by alkyl, alkoxy, halogen, or alkyl substituted by halogen, and alkyl, alkoxy and the alkyl moiety of aryloxy alkyl have 1 to 6 atoms;

R^2 is H or an alkyl group having 1 to 6 carbon atoms;

R^3 is H, alkyl, hydroxy, amino, cyano or acyl, wherein alkyl and acyl have 1 to 6 carbon atoms;

n is an integer of 1 to 6,

and wherein

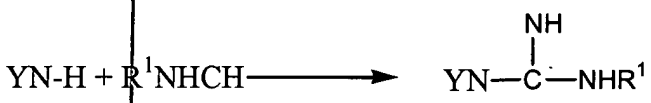
R^1 and R^3 may together complete a ring, comprising the steps of

(a) Reaction of a compound of formula (IV)

YN-H

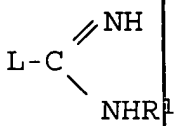
(IV)

with a cyanamide, R^1NHCN, according to the equation



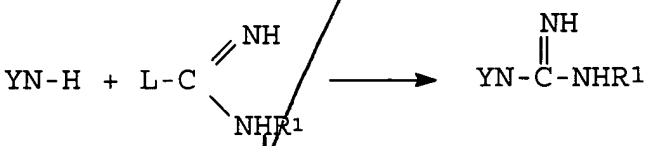
or

(b) Reaction of a compound of formula (IV) with a compound of formula (V)

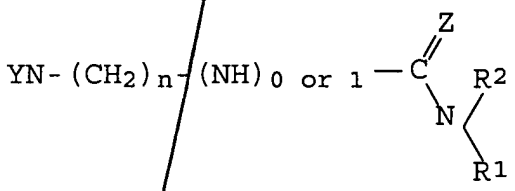


(V)

wherein L is a leaving group, according to the equation



20. (Twice Amended) A method for the preparation of a compound of formula II



(II)

in which

YN-represents an organic residue obtained by removal of the R group from an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine of formula (IIIa)

YN-R

(IIIa)

wherein R is H, alkyl of 1 to 6 carbon atoms, or cyclopropylmethyl,

Z is O, S or NR^3;

R^1 is H, alkyl or aryloxyalkyl, wherein the aryl group is optionally substituted by alkyl, alkoxy, halogen, or alkyl substituted by halogen, and alkyl, alkoxy and the alkyl moiety of aryloxy alkyl have 1 to 6 carbon atoms;

R^2 is H or an alkyl group having 1 to 6 carbon atoms;

R^3 is H, alkyl, hydroxy, amino, cyano or acyl, wherein alkyl and acyl have 1 to 6 carbon atoms;

n is an integer of 1 to 6,

and wherein

R^1 and R^3 may together complete an addition ring,

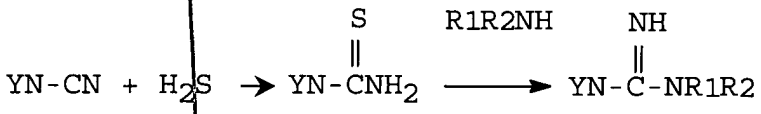
comprising the steps of

(a) Reaction of a compound of formula (VI)

YN-CN

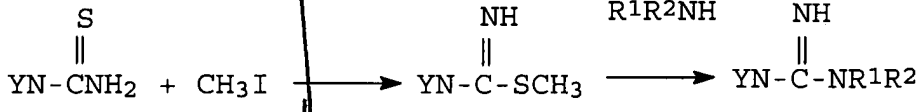
(VI)

with H_2S to obtain an N-thiocarboxamide YN-$CSNH_2$, and optionally reacting the YN-$CSNH_2$ with an amine R^1R^2NH according to the first stage or optionally the two stages of the equation

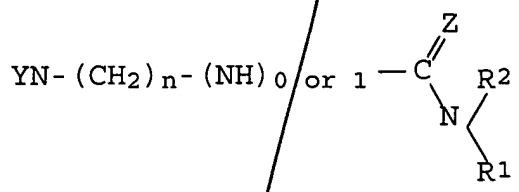


to yield a compound of formula II where Z is S if the optional step is not taken, or a compound of formula II where Z is NH if the optional step is taken, or

(b) Methylating the N-thiocarboxamide to yield an isothiourea compound, which is in turn reacted with an amine R^1R^2NH:



21. (Twice Amended) A method of synthesis of a compounds of formula (II)



(II)

in which

YN-represents an organic residue obtained by removal of the R group from an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine of formula (IIIa)

YN-R

(IIIa)

wherein R is H, alkyl of 1 to 6 carbon atoms, or cyclopropylmethyl,

Z is O, S or NR^3;

R^1 is H, alkyl or aryloxyalkyl, wherein the aryl group is optionally substituted by alkyl, alkoxy, halogen, or alkyl substituted by halogen, and alkyl, alkoxy and the alkyl moiety of aryloxy alkyl have 1 to 6 carbon atoms;

R^2 is H or an alkyl group having 1 to 6 carbon atoms;

R^3 is H, alkyl, hydroxy, amino, cyano or acyl, wherein alkyl and acyl have 1 to 6 carbon atoms;

n is an integer of 1 to 6,

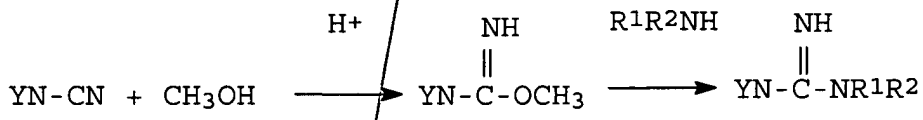
and wherein

R^1 and R^3 may together complete an addition ring,

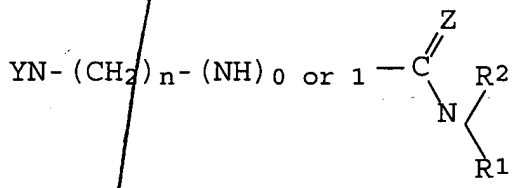
comprising the step of reacting an N-cyano compound of formula (VI)

YN-CN

with methanol under acidic conditions to yield an isourea, which in turn is reacted with an amine according to the equation



22. (Twice Amended) A method of synthesis of a compound of formula (II)



(II)

in which

YN-represents an organic residue obtained by removal of the R group from an opioid selected from the group consisting of morphine, codeine, heroin, ethylmorphine, O-carboxymethylmorphine, O-acetylmorphine, hydrocodone, hydromorphone, oxymorphone, oxycodone, dihydrocodeine, thebaine, metopon, ethorphine, acetorphine, diprenorphine (M5050), buprenorphine, phenomorphan, levorphanol, pentazocine, eptazocine, metazocine, ethoheptazine, ketobemidone, dihydroetorphine and dihydroacetorphine of formula (IIIa)

YN-R

(IIIa)

wherein R is H, alkyl of 1 to 6 carbon atoms, or cyclopropylmethyl,

Z is NH;

R^1 is H, alkyl or aryloxyalkyl, wherein the aryl group is optionally substituted by alkyl, alkoxy, halogen, or alkyl substituted by halogen, and alkyl, alkoxy and the alkyl moiety of aryloxy alkyl have 1 to 6 carbon atoms;

R^2 is H or an alkyl group having 1 to 6 carbon atoms;

n is an integer of 1 to 6,

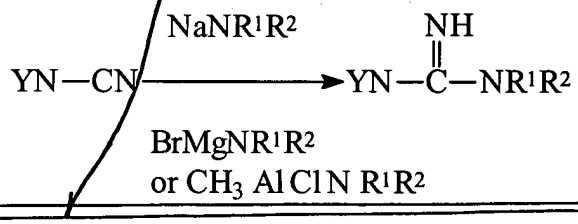
and wherein

R^1 and R^3 may together complete an addition ring,

comprising the step of reacting an N-cyano compound of formula (VI)

YN-CN

and a metallated residue



31. (New) A composition comprising a compound according to Claim 7, together with a pharmaceutically acceptable carrier.

32. (New) A method of inducing analgesia in a mammal, said method comprising administration of a compound of claim 1 in amounts effective to induce said analgesia.

33. (New) A method of inducing analgesia in a mammal, said method comprising administration of a pharmaceutical of claim 23 in amounts effective to induce said analgesia.